



# Cholinergic–Anticholinergic Drug Interactions

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Recently we described some of the pitfalls associated with categorizing potential drug interactions based upon the pharmacologic class of the drugs involved (*Pharmacy Times*, June 2005). Several instances exist, however, where a drug's pharmacologic class accurately predicts potential pharmacodynamic interactions. For example, many computerized drug interaction screening programs contain algorithms to detect duplicative therapy that are based on pharmacologic activity. The entry of an order for >1 nonsteroidal anti-inflammatory drug or diuretic agent may be flagged as duplicative prescribing. The risk of excess pharmacodynamic response and possible toxicity is the rationale for these warnings.

Drugs with anticholinergic activity can produce significant adverse responses when administered in combination. Drugs such as atropine and scopolamine inhibit muscarinic acetylcholine receptors and can produce both peripheral (constipation, dry mouth, tachycardia, urinary retention, reduced sweating) and central (cognitive and memory impairment, confusion, delirium, headache, blurred vision, dizziness, and drowsiness) effects. The concurrent administration of drugs with anticholinergic activity can cause a wide array of symptoms, particularly in elderly patients who are especially susceptible, due to age-related decrements in endogenous acetylcholine. Many drugs are noted in their labeling to have anticholinergic properties, and a few have been compared at fixed concentrations using in vitro receptor assays.<sup>1</sup> Limited

data are available comparing the anticholinergic potency of commonly used drugs under standard dosing conditions, but it seems reasonable to assume that combinations of these drugs will produce additive anticholinergic effects and possibly adverse reactions.

When drugs from opposing pharmacologic classes are coprescribed, an antagonistic response may occur, reducing the pharmacodynamic response of one or both drugs. The coadministration of anticholinergic agents with cholinergic drugs has been shown to inhibit the efficacy of the cholinergic agents.

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Patients with Alzheimer's disease being treated with cholinesterase inhibitors (eg, tacrine [Cognex], donepezil [Aricept], rivastigmine tartrate [Exelon], galantamine HBr [Razadyne]), plus drugs with anticholinergic activity, had a greater decline in their mental status when tested after taking concurrent anticholinergic drugs for 2 years.<sup>2</sup> It would seem obvious to avoid this combination. Two recent studies of patients taking cholinesterase inhibitors, however, found that anticholinergic drugs were coadministered in 33% to 35% of the patients.<sup>3,4</sup> While anticholinergic drugs may have been added to treat cholinesterase inhibitor side effects, this combination will likely result in reduced therapeutic efficacy of the cholinesterase inhibitor and perhaps the anticholinergic drug. Various cases have been noted of patients developing cognitive impairment when administered tolterodine tartrate (Detrol LA) or oxybutynin chloride (Ditropan XL)

while on cholinesterase inhibitor therapy for Alzheimer's disease. Other agents used for overactive bladder (trospium chloride [Sanctura], solifenacin succinate [Vesicare], and darifenacin [Enblex]) have anticholinergic activity and are likely to interact with cholinergic drugs in a similar manner.

The concurrent use of olanzapine (Zyprexa) in patients with Alzheimer's disease was associated with a dose-dependent increase in anticholinergic activity, compared with patients taking risperidone (Risperdal).<sup>5</sup> As with antidepressants, the selection of drugs to treat psychosis in patients with Alzheimer's disease should be made after consideration of potential pharmacodynamic interactions. The avoidance of drugs with anticholinergic properties (eg, bladder antispasmodics, sedating antihistamines, tricyclic antidepressants) minimizes the risk of cognitive impairment or other central nervous system side effects in patients with Alzheimer's disease.

Pharmacists need to be alert for potential interactions between drugs that have opposing pharmacologic properties because these combinations may not be identified by some computer screening systems. Since these interactions may result from attempts to treat drug side effects, changing or adjusting the dose of the drug responsible for the side effects should be considered when selecting a management strategy. This approach may eliminate the need for the interacting agent. When opposing drugs are prescribed for unrelated reasons, a reduction in the efficacy of one or both agents is likely to result. 

*For a list of references, send a stamped, self-addressed envelope to: References Department, Attn. A. Stahl, Pharmacy Times, 241 Forsgate Drive, Jamesburg, NJ 08831; or send an e-mail request to: [astahl@ascendmedia.com](mailto:astahl@ascendmedia.com).*